A STUDY OF TOBACCO CARCINOGENESIS

II. Dose-Response Studies

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Since epidemiological studies have repeatedly shown that the risk of lung cancer increases in proportion to the increase in the amount of tobacco used, it is important to know the level below which tobacco-smoke condensate ("tar") would not significantly influence the development of cancer. Such a "threshold" level in man has been suggested by statistical studies.[1-3] It was thought pertinent to determine it in the laboratory animal. If reduction to such a level is possible and practical, effective preventive measures may be at hand.

METHODOLOGY

The methods of cigarette-tar collection and application were the same as those previously described.[3]

The 520 Swiss (Millerton) mice used in this study were divided into groups for the investigation of certain variables:

Variation in Concentration. All mice in groups 1 to 11 were painted with a 1:1 tar-acetone solution. Group-12 mice were painted with a 1:2 solution. Two experimental groups painted with 1:3 and 1:4 solutions respectively are still being studied. The mice in groups painted with a 1:1 tar-acetone solution received approximately 65 mg. per painting, and those in the group painted with a 1:2 solution, approximately 43 mg. per painting.

Variation in Frequency. Group-1 mice were painted five times a week, group-2 three times a week, group-3 two times a week, and group-4 once a week. Group-5 mice were painted three times a week for alternating two-week periods. Group-6 mice were painted three times a week for alternating four-week periods. Mice in groups 7 to 12 were painted three times a week.

Variation in Duration. Mice in groups 1 to 6 and those in groups 11 and 12 were painted for their entire life span. Painting was stopped after periods of three, six, nine, and twelve months respectively for groups 7 to 10.

The present experiment thus studied groups of mice receiving varying amounts of tar. By determining the total number of tumors developed and the latent periods before tumor developments, the relative activities of the various tar concentrations and painting schedules were evaluated.

It is realized that the term "dose" does not have the same meaning in this study that it has in an experiment in which one injects a known amount of carcinogen into an animal or applies an exact amount of carcinogen to the skin. With the skin-painting technique used here, one can obtain only an approximate idea of the amount of a substance given to each animal. However, this type of application of carcinogen approximates that to which the human is exposed, and, more important than the evaluation of a given single experimental group, it enables one to make a comparison from group to group.

RESULTS

A decrease in the frequency of tar application was followed by a significant decline in the number of tumors formed and an increase in the latent periods before tumor formation (Table 1). Only one cancer (an incidence of 5 per cent) was produced in the mice painted twice a week (group 3). This occurred in the fourteenth month. In the mice painted three times a week (group 2), eight cancers were produced, with the first one appearing in the eight month. In the mice receiving tar once a week (group 4), only two papillomas developed. The high mortality among mice painted five times a week (group 1) makes this frequency of painting impractical. At the end of one year of tar application, only 18 per cent of the mice in this group were still alive. There was no indication that tumor formation was speeded up in this group.

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The statistical analysis of these data was carried out with the assistance of Dr. Irwin J. Bross and Mrs. Rivkah Feldman.

Received for publication May 23, 1957.